# METHODS, SYSTEMS AND COMPUTER PROGRAM PRODUCTS FOR SELECTIVELY INITIATING INTERVENTIONAL THERAPY TO REDUCE THE RISK OF ARRHYTHMIA

## Field of the Invention

The present invention relates to cardiac therapy, and more specifically to antiarrhythmic therapies.

## Background of the Invention

Despite advances in antiarrhythmic therapies, cardiac arrhythmias remain a major health problem, causing about 300,000 sudden cardiac deaths annually in the United States (Weiss JN et al., Circulation (1999) 99:2819-2826). Cardiac arrhythmias can occur when the electrical waves which stimulate the heart meander erratically through the heart muscle, creating disordered and ineffective contraction. The primary focus of literature and research has been on detecting when cardiac arrhythmias occur and reducing the occurrence of arrhythmias with medical therapies or lifestyle changes. Medical therapies include drugs which can reduce the occurrence of arrhythmias and implantable devices which can detect the onset of arrhythmias and apply electrical pulses to the heart to stop arrhythmias.

## Summary of the Invention

According to embodiments of the present invention, methods, systems, and computer program products for selectively initiating interventional therapy in a subject are provided. Electrical activity can be chronically detected in first and second cardiac regions in the subject. Discordant alternans in at least one component of the detected electrical activity can by identified. Interventional therapy can be initiated in the subject responsive to the identification of discordant alternans.

Identifying discordant alternans can be based on cycle-to-cycle variations in the detected electrical activity. In some embodiments, the component in which discordant alternans is detected includes a duration and/or amplitude of an STT segment. Initiating interventional therapy can be responsive to a change in the component from concordant to discordant alternans. The interventional therapy may reduce the risk of arrhythmia, including the risk of ventricular arrhythmia and/or atrial

arrhythmia. For example, the interventional therapy may introduce a pacing routine, administer a shock, and/or administer a drug that reduces a risk of arrhythmia.

In some embodiments, the electrical activity comprises an ECG signal from external electrodes and/or an electrogram from internally implanted electrodes. The component can be the duration of a cardiac signal component, the amplitude of a cardiac signal component, and/ or the shape of a cardiac signal component.

As will further be appreciated by those of skill in the art, while described above primarily with reference to method aspects, the present invention may be embodied as methods, apparatus/systems and/or computer program products.

## Brief Description of the Drawings

**Figure 1** is a block diagram of a device according to embodiments of the present invention;

**Figure 2** is a block diagram of operational circuitry according to embodiments of the present invention;

**Figure 3** is a block diagram of operational circuitry and/or computer program modules suitable for carrying out operations according to embodiments of the present invention;

**Figure 4** is a schematic illustration of an implantable apparatus with exemplary electrode placements according to embodiments of the present invention;

**Figure 5** is a flowchart illustrating operations that can be carried out according to embodiments of the present invention; and

**Figure 6** is a graph of cardiac cycles illustrating concordant and disconcordant alternans according to embodiments of the present invention.

## Detailed Description of Embodiments of the Invention

The present invention will now be described more fully hereinafter with reference to the accompanying figures, in which embodiments of the invention are shown. This invention may, however, be embodied in many different forms and should not be construed as limited to the embodiments set forth herein. Like numbers refer to like elements throughout. In the figures, certain regions, components, features or layers may be exaggerated for clarity. Broken lines where used indicate optional features, components or operations. It will be understood that when an element is referred to as being "coupled" or "connected" to another element, it can be directly

coupled or connected to the other element or intervening elements may also be present. In contrast, when an element is referred to as being "directly coupled" or "directly connected" to another element, there are no intervening elements present.

The flowcharts and block diagrams of certain of the figures herein illustrate the architecture, functionality, and operation of possible implementations for predicting arrhythmias and/or selectively initiating interventional therapy according to the present invention. In this regard, each block in the flow charts or block diagrams represents a module, segment, or portion of code, which comprises one or more executable instructions for implementing the specified logical function(s). It should also be noted that in some alternative implementations, the functions noted in the blocks may occur out of the order noted in the figures. For example, two blocks shown in succession may in fact be executed substantially concurrently or the blocks may sometimes be executed in the reverse order, depending upon the functionality involved. In addition, some functions noted in the blocks may be combined or separated. While the present invention is illustrated in certain of the figures with reference to particular divisions of programs, functions and memories, the present invention should not be construed as limited to such logical divisions. Thus, the present invention should not be construed as limited to the configuration of operation as shown in the figures, but is intended to encompass any configuration capable of carrying out the operations described herein.

The present invention is intended primarily for use on human subjects, but may optionally be carried out on other mammalian subjects for veterinary purposes.

Referring to **Figure 1**, an exemplary cardiac device **10** is shown. The device **10** includes a housing **13**, a power source **12** held in the housing **13**, and a controller **14** held in the housing **13** and operatively associated with the power source **12**. A signal analyzer **18** is operatively associated with the controller **14** and receives a signal that represents electrical activity in the heart of a subject **20**. The signal analyzer **18** analyzes a cardiac signal and determines if a therapy should be initiated and/or administered to the subject **20** by a therapy module **16**.

Accordingly, electrical activity in the heart of a subject can be chronically detected and interventional therapy can be selectively administered. Chronic detection of electrical activity refers to the detection of electrical activity over an extended duration of time. The detection of electrical activity is not necessarily continuous and interruptions in detection may occur; however, in some embodiments, continuous

detection of electrical activity may be provided. In some embodiments, electrical activity for successive cardiac cycles can be detected from a system chronically implanted in a subject.

Referring to **Figure 1**, signals representing electrical activity in more than one cardiac region in the subject can be received by the signal analyzer **18**. The signal analyzer **18** can identify discordant alternans in at least one component of the detected electrical activity, for example, by comparing a component of the signal received from two or more cardiac regions over cardiac cycle(s). Alternans is a change in the amplitude and/or morphology of a component of electrical activity in the heart, such as in an electrocardiogram (ECG), that occurs on an alternating basis, such as every-other-beat. Discordant alternans is alternans that occur on an alternating basis at different cardiac regions. According to embodiments of the present invention, interventional therapy can be initiated in the subject responsive to the identification of discordant alternans, for example, by detecting a relative change in the component at the cardiac regions either between different sensing locations in the same cycle or the same location over different cycles. For example, if the signal analyzer **18** detects a relative change in a component of the electrical signal at the cardiac regions, then the therapy module **16** can deliver a therapeutic treatment to reduce a risk of arrhythmia. In some embodiments, the relative change can be a millivolt change or smaller. Further examples of detection methods can be found, for example, in U.S. Patent Nos. 4,802,491 and 5,148,812, the disclosures of which are incorporated by reference in their entireties.

As an overview of a cardiac signal and examples of cardiac components, the driving force for the flow of blood in the heart comes from the active contraction of the cardiac muscle. An electrical signal causes this contraction of the heart. The electrical signals described herein can be detected as an ECG signal from external electrodes situated on the surface of the patient and/or from internally implanted electrodes. Electrical signal components from external and/or internal electrodes can be used to detect alternans. The cardiac contraction is triggered by electrical impulses traveling in a wave propagation pattern, which begins at the cells of the sinoatrial node and the surrounding atrial myocardial fibers, and then traveling into the atria and subsequently passing through the atrioventricular node and, after a slight delay, into the ventricles.

The beginning of a cardiac cycle is initiated by a P wave, which is normally a small positive wave in the body surface electrocardiogram. The P wave induces

depolarization of the atria of the heart. The P wave is followed by a cardiac cycle portion which is substantially constant with a time constant on the order of 120 milliseconds ("ms").

The "QRS complex" of the cardiac cycle occurs after the substantially constant portion. The dominating feature of the QRS complex is the R wave which is a rapid positive deflection. The R wave generally has an amplitude greater than any other wave of the cardiac cycle, and has a spiked shape of relatively short duration with a sharp rise, a peak amplitude, and a sharp decline. The QRS complex is the depolarization of the ventricles and therefore, the term "ventricle activations" denotes a QRS complex of the cardiac cycle. The QRS complex is completed by the S wave, which is typically a small deflection that returns the cardiac signal to baseline.

Following the S wave, the T wave occurs after a delay of about 250 ms. The T wave is relatively long in duration (*e.g.,* about 150 ms). The cardiac cycle between the S wave and the beginning of the T wave is commonly referred to as the ST segment. The STT segment refers to the cardiac cycle between the S wave and the end of the T wave. The T wave is a sensitive part of the cardiac cycle, during which an electrical stimulus, such as an atrial defibrillation shock, is to be avoided, in order to reduce the possibility of induced (and often fatal) ventricular fibrillation. The next cardiac cycle begins with the next P wave. The typical duration of a complete cardiac cycle is on the order of about 800 ms.

In some embodiments, an electrogram recorded from an electrode on or in the heart can be used to detect alternans. Such an electrogram can include an activation complex and a repolarization complex. The activation complex can be referred to as a QRS or RS complex and may be recognized as a rapid downslope in a recording from a unipolar electrode and as a spike in a recording from a bipolar electrode. The repolarization complex may be referred to as a T wave and may be more prominent in a unipolar than in a bipolar recording. The activation recovery interval (ARI) is a measurement proportional to the refractory period and to the action potential duration of the tissue around the electrode. The ARI can be calculated as the time from the fastest downstroke of the activation complex of the unipolar electrogram to the fastest upstroke of the T wave of the unipolar electrogram.

Accordingly, any cardiac signal component (e.g., STT segment, R wave, T wave, ARI, QRS complex, etc.) can be identified to detect alternans. Moreover, various characteristics of cardiac signal components can be used to detect alternans,

including the duration of a cardiac signal component, the amplitude of a cardiac signal component, the shape of a cardiac signal component, and the like. Alternans can also include alternating patterns having periods of varying lengths. For example, a characteristic of a component in the cardiac signal used to identify discordant alternans can repeat ever other beat, every fourth beat, every sixth beat and so on.

An exemplary graph of STT segment duration and amplitude illustrating a general pattern including cycle-to-cycle STT segments having no alternans, concordant alternans, and discordant alternans is shown in **Figure 6**. In concordant alternans, different portions of the myocardial region exhibiting alternans are in phase with one another. That is, electrical signals detected at different points in the myocardial region each exhibit the same alternating pattern from beat to beat if a patient is experiencing concordant alternans. For example, as shown in **Figure 6**, a taller (*i.e.*, greater amplitude) or longer duration STT segment can alternate beat to beat with a smaller (*i.e.*, smaller amplitude) or shorter duration STT segment simultaneously at different myocardial spatial regions. However, in the case of discordant alternans, different portions of the myocardial region can be out of phase with one another. For example, one portion of the myocardium can exhibit a taller or longer STT segment while another portion exhibits a smaller or shorter STT segment during the same beat. In the next beat, the relative amplitude or duration of the STT segment is reversed. That is, the portion of the myocardium exhibiting the longer STT segment during the previous beat next exhibits a shorter STT segment, and the portion that exhibited the shorter STT segment during the first beat exhibits a longer STT segment in the second beat. Various other components of a cardiac signal can be used to detect discordant alternans.

Without wishing to be bound by any particular theory, it is believed that changes in cardiac signal components (*e.g.*, STT segment duration and/or amplitude) of a cardiac cycle over time in which comparisons between different cardiac locations can diverge, such as in the onset of discordant alternans, may indicate a heightened risk of arrhythmia. Accordingly, the risk of arrhythmia may be predicted and/or reduced with interventional therapy prior to the onset of arrhythmia. Embodiments of the present invention may be applied to various forms of cardiac tachyarrhythmias, including atrial and ventricular fibrillation, with defibrillation (including cardioversion) shocks or pulses and/or pacing routines. Examples include the prevention and/or treatment of

polymorphic ventricular tachycardia, monomorphic ventricular tachycardia, ventricular fibrillation, atrial flutters, and atrial fibrillation.

As shown in **Figure 1**, the therapy module **16** is configured to deliver one or more therapeutic treatments to reduce a risk of arrhythmia responsive to a relative change in a cardiac signal component as determined by the signal analyzer **18**. Any suitable interventional therapy may be used, including therapies that reduce the risk of atrial and/or ventricular arrhythmia, such as administering a pacing routine, an electrical shock (such as a defibrillation shock), or a drug. Examples of drugs that can be used include calcium channel blockers, calmodulin blockers, calmodulin kinase inhibitors, beta blockers and antiarrhythmic drugs. Examples of drug delivery systems are provided in co-assigned Application Serial No. 10/071,269, entitled *Methods and Devices for Treating Arrhythmias Using Defibrillation Shocks*, filed February 8, 2002, the disclosure of which is incorporated by reference in its entirety. The therapy module **16** can automatically deliver a therapeutic treatment to reduce the risk of arrhythmia, for example, by automatically delivering a pacing routine, a defibrillation shock and/or a therapeutic drug. The treatment can also be delivered manually. For example, in some embodiments, the therapy module **16** notifies a user, such as a health care professional or the patient, that a therapeutic treatment should be administered to the patient.

Various pacing routines, including pacing routines known to those of skill in the art, can be used. For example, the pacing routines can include one or more pulses from electrodes in various cardiac locations, including electrodes that can also be used to detect alternans and/or the electrode configuration shown in **Figure 4**. Pacing routines can be administered as a single pulse or a series of pulses from one or more electrodes. Pacing routines can also be administered simultaneously from multiple electrodes. In some embodiments, the pacing routine can be timed based on the spatial and/or temporal pattern of the detected alternans. For example, a pacing routine can be timed to stimulate a cardiac region coinciding with the detection of a shorter STT segment in the same region. The pacing routine could also be timed to stimulate a cardiac region during or after a beat exhibiting a shorter or longer STT segment.

The device **10** can be an external or internal device. Accordingly, the signal analyzer module **18** can receive electrical activity of the heart from internal electrodes by an implantable anti-arrhythmic device or from external electrodes by an external anti-arrhythmic device. Moreover, the therapy module **16** can administer a pacing routine or defibrillation shock from internal or external electrodes. In the case of drug therapies,

the therapy module **16** can administer a drug automatically from an internally implantable drug delivery system as described, for example, U.S. Application Serial No. 10/071,269. Interventional therapies can be administered alone or in combination with other therapies. For example, a pacing routine and/or defibrillation shock can be administered before, at the same time, or after a drug is delivered.

**Figure 2** illustrates a device **150** according to further embodiments of the invention, which contains an electronic circuit **15**. The electrical circuit **15** can include circuitry that can sense or detect electrical signals in a cardiac region (*e.g.*, from electrodes positioned to sense the electrical signals in the cardiac region), analyze the electrical signals, and/or control the delivery of appropriate therapies, such as shocks to the cardiac region (such as defibrillation shocks and/or pacing routines) and/or drug delivery.

As illustrated in **Figure 2**, the electrical circuit **15** includes leads **84** that are electrically connected to external and/or internal electrodes (**Figure 4**) placed in electrical contact with a heart, a switch **82** for controlling signals to and from the leads **84**, an atrial and/or ventricular detector **70** that receives and analyzes cardiac signals that are received by the leads **84,** and a cardiac cycle monitor or "synchronization monitor **72**") for providing synchronization information to a controller **74**. The controller **74** controls a shock generator **79,** which includes a capacitor charging circuit **76** that charges the storage capacitor **78** to a predetermined voltage, typically from a power source such as a battery source (not shown). The controller **74** can direct a discharge circuit **80** to discharge an electrical current from the shock generator **79** to the switch **82** into leads **84**. Accordingly, leads **84** can provide electrical sensing and/or shocking functionality. The controller **74** also includes a discordant alternans module **100** and a therapy module **125**. The controller **74** also controls a drug delivery system **140** for delivering a drug and a pacing system **130** for monitoring cardiac cycles from the electrical signals from the heart sensed by the electrodes and for providing a pacing routine.

Still referring to **Figure 2**, generally described in operation, upon receiving a signal from the leads **84** and the detector **70**, the discordant alternans module **100** of the controller **74** analyzes the signal. The signal can represent electrical activity in two or more cardiac regions. The discordant alternans module **100** compares a segment in a cardiac cycle represented by the electrical activity at the cardiac regions. The therapy module **125** initiates and/or controls the administration of an interventional therapy

responsive to a relative change in the component at the two cardiac regions. The relative change in the component can be monitored over a plurality of cardiac cycles to detect cycle-to-cycle variations that can indicate that therapy is needed. The administered therapy can be a defibrillation shock, a pacing routine, and/or a delivery of a drug. For example, in some embodiments, the therapy module **125** can direct a drug to be delivered from the drug delivery system **140**, a pacing routine to be delivered from the pacing system **130**, and/or a shock to be delivered from the shock generator **79**. Moreover, the pacing system **130** can communicate with the shock generator **79** to control a pacing routine delivered to leads **84** via the switch **82**.

For example, the therapy module **125** can signal the shock generator **79** to generate a defibrillation shock and/or pacing routine having particular characteristics. The capacitor charging circuit **76** of the shock generator **79** charges the storage capacitor **78** to a predetermined voltage. The storage capacitor **78** can be 20 to 400 microfarads in size, and may be a single capacitor or a capacitor network (e.g., separate pulses can be driven by the same or different capacitors). The discharge of the capacitor **78** may be controlled by the controller **74** and/or a discharge circuit **80**. The controller **74**, based on information from the synchronization monitor **72**, can direct the shock to be relayed to either the discharge circuit **80** for further processing (*i.e.*, to further shape the waveform signal, time the pulse or pulses, etc.) or directly to an output lead or to a switch, such as switch **82**. The controller **74** may also control the desired or proper selection of predetermined defibrillation electrode pair(s), where multiple defibrillation electrodes are used, to direct the switch **82** to electrically activate a desired electrode pair to align the predetermined electric shock pulse pathway through which the shock pulse is provided. As an alternative, the therapy module **125** can provide an alert to administer the shock profiles and/or pulse sequences. For example the therapy module can provide a local or remote audible and/or visual alert to a patient or to a health care professional.

In some embodiments, the pulse generator includes a single capacitor **78**, and the controller **74** includes a switch (*e.g.*, a crosspoint switch) operatively associated with that capacitor. Various shock profiles and/or shock sequences can be used. For example, the controller **74** may be configured to provide a shock profile consisting of a biphasic pulse (*i.e.*, a first phase of a pulse of a predetermined polarity followed by a second phase of a pulse of reversed polarity). Single pulses and/or sequences of pulses, including monophasic, biphasic, and/or triphasic pulses may also be used. Various shock profiles may be used having various properties including waveform, duration, polarity, shape,

periodicity, energy, voltage, etc. Exemplary shock profiles are described in U.S. Pat. No. 6,327,500 to Cooper et al., 5,978,705 to KenKnight et al. U.S. Patent Application Serial Number 10/012,115 (Publication No. 02 0161407) filed November 13, 2001, the contents of which are hereby incorporated by reference as if recited in full herein.

The controller **74** can deliver a preselected electrical pulse to predetermined electrode pairs through a switch **82**. The shock generator **79** (including a capacitor charger **76**, capacitor **78**, and discharge circuit **80**), controller **74,** and switch **82** thus work in concert to produce and deliver a pulse having a particular shock profile. Therefore, it will be appreciated that in operation, in response to an input from the detector **70**, the discordant alternans module **100** and/or the therapy module **125**, the controller **74** controls the pulse or shock generator **79** to synchronize the delivery of the timed pulse output to the proper electrode pair in accordance with the cardiac cycle information received from the synchronization monitor **72** and the specific electrode configuration employed by or selected by the device. Further, when employing a biphasic waveform, it will be appreciated by those of skill in the art that the pulse or shock generator **79** can also include a crosspoint switch to switch the polarity of the electrode pair for delivery of the second (inverted or negative) waveform phase. The electronic package may also include a receiver/transmitter coupled to the internal controller **74** for communicating with an external controller. Thus, the pulse regimen could be altered by external input to the controller to alter, for example, the waveform, the voltage, the electrode coupling, or even to retrieve monitoring data received and stored in memory about the number of atrial fibrillation episodes and the effectiveness of the shock level.

In some embodiments, the switch **82** is programmable (*e.g.,* by remote control such as by a radio signal) to alter the coupling of the pulse generator to the atrial defibrillation electrodes. This feature may be particularly suitable when multiple electrodes are implanted so that the electrode pairs that deliver the shocks may be changed to optimize the technique for a particular patient.

The electrical circuit **15** can include one or more amplifiers (not shown) for amplifying the sensed cardiac signals. Defibrillation and/or pacing electrodes may be configured to sense cardiac cycles from electrical signals from the heart, or may have smaller sensing electrodes placed adjacent thereto and thereby provide input to the electronics package as well as provide a predetermined stimulation shock output to predetermined cardiac areas as directed by the controller **74**. The synchronization

monitor **72** can provide additional assurance that defibrillation shock pulses are not delivered during sensitive portions of the cardiac cycle so as to reduce the possibility of inducing ventricular fibrillation.

The present invention should not be construed as limited to the configuration of **Figure 2**, which is intended to encompass any configuration capable of carrying out the operations described herein, including implantable and external configurations.

**Figure 3** is a block diagram of exemplary embodiments of data processing systems that illustrates systems, methods, and computer program products in accordance with embodiments of the present invention. The data processing system **305** includes a processor **310** that can send and receive information to or from a sensing system **325** and a shock generation system **320** and/or a drug delivery system **340**. The data processing system **305** may be implemented externally or internally with respect to the patient. The shock generation system **320** and/or the sensing system **325** may be implanted in the patient or be implemented externally.

The processor **310** communicates with the memory **314** via an address/data bus **348**. The processor **310** can be any commercially available or custom microprocessor. The memory **314** is representative of the overall hierarchy of memory devices containing the software and data used to implement the functionality of the data processing system **305**. The memory **314** can include, but is not limited to, the following types of devices: cache, ROM, PROM, EPROM, EEPROM, flash memory, SRAM, and DRAM.

As shown in **Figure 3**, the memory **314** may include several categories of software and data used in the data processing system **305**: an operating system **352**; application programs **354**; input/output (I/O) device drivers **358**; a discordant alternans module **360**, a therapy module **362** and data **356**. The data **356** may include electrical activity data **350**, such as an ECG signal or electrogram, which may be obtained from a electrical sensor for detecting electrical activity in the cardiac region, for example, from the sensing system **325**.

As will be appreciated by those of skill in the art, the operating system **352** may be any operating system suitable for use with a data processing system, such as OS/2, AIX, OS/390 or System390 from International Business Machines Corporation, Armonk, NY, Windows CE, Windows NT, Windows95, Windows98 or Windows2000 from Microsoft Corporation, Redmond, WA, Unix or Linux or

FreeBSD, Palm OS from Palm, Inc., Mac OS from Apple Computer, or proprietary operating systems. The I/O device drivers **358** typically include software routines accessed through the operating system **352** by the application programs **354** to communicate with devices such as I/O data port(s), data storage **356** and certain memory **314** components and/or the shock generation system **320,** sensing system **325** and/or drug delivery system **340**. The application programs **354** are illustrative of the programs that implement the various features of the data processing system **305** and preferably include at least one application which supports operations according to embodiments of the present invention. Finally, the data **356** represents the static and dynamic data used by the application programs **354**, the operating system **352**, the I/O device drivers **358**, and other software programs that may reside in the memory **314.**

While the present invention is illustrated, for example, with reference to the discordant alternans module **360** and the therapy module **362** being an application program in **Figure 3**, as will be appreciated by those of skill in the art, other configurations may also be utilized while still benefiting from the teachings of the present invention. For example, the discordant alternans module **360** and/or the therapy module **362** may also be incorporated into the operating system **352**, the I/O device drivers **358** or other such logical division of the data processing system **305**. Thus, the present invention should not be construed as limited to the configuration of **Figure 3**, which is intended to encompass any configuration capable of carrying out the operations described herein.

The I/O data port can be used to transfer information between the data processing system **305** and the shock generation system **320**, sensing system **325**, or another computer system or a network (*e.g.*, the Internet) or to other devices controlled by the processor. These components may be conventional components such as those used in many conventional data processing systems that may be configured in accordance with the present invention to operate as described herein.

Accordingly, the sensing system **325** can send an electrical signal, such as an ECG or electrogram signal, to the processor **310**. The electrical signal can be stored as electrical activity data **350**. The discordant alternans **360** can compare electrical signals at different positions in the cardiac region to determine relative changes, such as variations in a single cycle between the positions, discordant alternans and other cycle-to-cycle changes. In response to a detected relative change, the therapy module **362** can initiate a therapy. For example, the therapy module **362** can instruct the shock

generation system **320** to administer a shock, such as a defibrillation shock and/or pacing routine. The therapy module **362** can instruct the drug delivery system **340** to deliver a therapeutic drug. In some embodiments, the therapy module **362** alerts a user, such as a health care professional, that interventional therapy should be administered. The therapy module **362** can also select one of several therapies based on the particular relative change detected by the discordant alternans **360**.

In some embodiments, various functionalities discussed herein can be implemented in an internally implantable system as shown in **Figure 4**, although as noted previous, external systems can also be used. Anatomically, the heart includes a fibrous skeleton, valves, the trunks of the aorta, the pulmonary artery, and the muscle masses of the cardiac chambers (*i.e.,* right and left atria and right and left ventricles). The schematically illustrated portions of the heart **230** illustrated in **Figure 4** includes the right ventricle "RV" **232**, the left ventricle "LV" **234**, the right atrium "RA" **36**, the left atrium "LA" **238**, the superior vena cava **248**, the coronary sinus "CS" **242**, the great cardiac vein **244**, the left pulmonary artery **245**, and the coronary sinus ostium or "os" **240**.

Referring to **Figure 4**, the device **210** can include an implantable housing **213** that contains a hermetically sealed electronic circuit, such as the circuit **15** as shown in **Figure 2**. The device **210** can be configured detect electrical activity and/or to administer defibrillation and/or pacing routines according to embodiments of the present invention. The housing **213** can include an electrode comprising an active external portion **216/H** of the housing, with the housing **213** preferably implanted in the left thoracic region of the patient (e.g., subcutaneously, in the left pectoral region) in accordance with known techniques as described in G. Bardy, U.S. Patent No. 5,292,338. As shown, the system can include a first catheter **220** and a second catheter **221**, both of which are insertable into the heart (typically through the superior or inferior vena cava) without the need for surgical incision into the heart. The term "catheter" as used herein includes "stylet" and "lead" interchangeably. Each of the catheters **220, 221** contains electrode leads wires **220a**, **220b**, **220c**, **221a'**, **221d**, **221e**, **221f**, and **220g** respectively, with the small case letter designation corresponding to the large-case letter designation for the defibrillation electrode to which each lead wire is electrically connected.

As illustrated in **Figure 4**, the catheter **220** includes electrodes **A50** and **G56** that reside in the right atrium "RA" (the term "right atrium" herein including the superior vena cava and innominate vein), an electrode **B51** positioned in the right ventricle

(preferably in the right ventricular apex), and an electrode **C52** positioned within the left pulmonary artery (the term "left pulmonary artery" herein includes the main pulmonary artery and the right ventricular outflow tract).

The second catheter lead **221** includes, from proximal to distal, an electrode **A50'** in the right atrium; an electrode **D53** positioned in the proximal coronary sinus, adjacent the coronary sinus ostium or "OS" **240**; an electrode **E55** positioned in the distal coronary sinus (preferably as far distal in the coronary sinus as possible) (the term "distal coronary sinus" herein includes the great cardiac vein); and an electrode **F56** at or adjacent the tip of the catheter in a coronary vein on the surface (preferably the posterolateral surface) of the left ventricle (e.g., in the lateral-apical left ventricular free wall). The position of electrode **F56** may be achieved by first engaging the coronary sinus with a guiding catheter through which a conventional guidewire is passed. The tip of the torqueable guidewire is advanced under fluoroscopic guidance to the desired location. The lead **221** on which electrode **F56** is mounted passes over the guidewire to the proper location. The guidewire is withdrawn and electrode **F56** is incorporated into the defibrillation lead system.

The active external portion of the housing **216** serves as an optional electrode **H**, which may be used for either atrial or ventricular defibrillation.

As illustrated in **Figure 4**, any or all of the electrodes can sense discordant alternan electrical signals and transmit the signals to the device **210**. The electrodes shown in **Figure 4** can also be configured to provide a defibrillation pulse, pacing routine and/or cardiac resynchronization therapy (CRT), and in some embodiments, an electrode can be used for providing both sensing and pulsing functionality. For example, in some embodiments, two electrodes configured for CRT can be used to detect alternans and/or deliver pulses, including defibrillation pulses, pacing routines, and/or CRT pulses. The two electrodes configured for CRT can be situated in the right and left ventricles according to known techniques. Moreover, it will be appreciated by those of skill in the art that various electrode configurations, including additional sensing and/or pulsing electrode(s) in alternative cardiac areas, can be used. Additional sensing electrodes may also be placed near defibrillation electrodes. In some embodiments, sensing electrodes can be used to provide sensing signals to sensor input lines to a detector in the device **210**. The sensing input can be used to compare cardiac signal components in a cardiac cycle, for example, using a discordant alternans module and/or signal analyzer as described herein. The electrodes can also be used to administer

interventional therapy, such as a defibrillation pulse and/or pacing routine, responsive to a relative change in cardiac signal components in different cardiac regions.

Numerous configurations of capacitor and control circuitry may be employed as described herein. Additional features can also be added to the device **210** including, for example, safety features such as noise suppression or multiple wave monitoring devices (R and T), verification checking to reduce false positive, precardioversion warning, programmed delayed intervention, bipolar configured sensing electrodes, intermittently activated defibrillation detector to reduce energy drain, a switching unit to minimize lines from the pulse generator, etc.

Those skilled in the art will appreciate that various electrode combinations are possible for both atrial and ventricular defibrillation and/or pacing by employing the "active can" electrode **H**, as discussed herein. In addition, multiple electrodes can be electrically coupled or "tied" together to form a single pole. For example, a shock can be delivered from either the RV or LV as one pole to the PA and OS tied together as the other pole.

Operations according to embodiments of the present invention are shown in **Figure 5**. A signal analyzer detects electrical activity at two cardiac regions in the subject at Block **500**. If discordant alternans are identified at Block **510**, then the signal analyzer triggers the administration of interventional therapy at Block **520**.

Systems as described above may be implanted in a patient by conventional surgical techniques, or techniques readily apparent to skilled surgeons in light of the disclosure provided herein, to provide an implanted defibrillation or cardioversion system. Embodiments may include surface mounted, internally implanted, or external components or a combination thereof.

Embodiments of the present invention are described herein with reference to "defibrillation" electrodes, "defibrillation" shocks, and the like. It should be understood that "defibrillation" electrodes and shocks include electrodes and shocks that reduce the risk of the occurrence of fibrillation as well as electrodes and shocks that result in actual defibrillation of a fibrillating heart. Accordingly, a defibrillation shock from a defibrillation electrode can be delivered without actual fibrillation being present.

Although the system has been primarily described above as an implantable system, it will be appreciated by those of ordinary skill in the art that the invention could also be incorporated into an external system which employs catheters to position the electrodes within a patient's heart or other desired configuration.

The foregoing is illustrative of the present invention and is not to be construed as limiting thereof. Although a few exemplary embodiments of this invention have been described, those skilled in the art will readily appreciate that many modifications are possible in the exemplary embodiments without materially departing from the novel teachings and advantages of this invention. Accordingly, all such modifications are intended to be included within the scope of this invention as defined in the claims. Therefore, it is to be understood that the foregoing is illustrative of the present invention and is not to be construed as limited to the specific embodiments disclosed, and that modifications to the disclosed embodiments, as well as other embodiments, are intended to be included within the scope of the appended claims. The invention is defined by the following claims, with equivalents of the claims to be included therein.